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(54) Title: **SUNSCREEN COMPOSITIONS CONTAINING A DIBENZOYLMETHANE DERIVATIVE AND A TRIAZINE DERIVATIVE**

(57) Abstract: The present invention relates to a composition comprising: (a) one or more dibenzoylmethane derivative UV-A absorbing agent(s) and (b) one or more triazine derivative(s); a method of stabilizing a dibenzoylmethane derivative UV-A absorbing agent in a composition comprising adding to said composition an effective amount of a triazine derivative, and a method of protecting mammalian skin or hair from UV radiation comprising topically applying to the skin or hair such a composition.

WO 02/17873 A1

**SUNSCREEN COMPOSITIONS CONTAINING A DIBENZOYLMETHANE
DERIVATIVE AND A TRIAZINE DERIVATIVE**

FIELD OF THE INVENTION

The present invention relates to sunscreen composition comprising a dibenzoylmethane derivative and having enhanced photostability.

BACKGROUND OF THE INVENTION

The prolonged exposure to UV radiation, such as from the sun, can lead to the formation of light dermatoses and erythemas, as well as increase the risk of skin cancers, such as melanoma, and accelerate skin aging, such as loss of skin elasticity and wrinkling. Both light having wavelengths in the UV-A range (from about 320 to 400 nm) and the UV-B range (from about 280 to about 320 nm) can cause such skin damage, and, thus, sunscreen compositions should preferably comprise both UV-A and UV-B absorbers/reflectors (UV sunscreens). Dibenzoylmethane derivatives, the most commonly used UV-A absorbers, however, often suffer from photochemical instability, requiring repeated application to the skin to maintain the desired UV-A protection. See, e.g., Kammeyer, et al., Int. J. Cosm. Sci. 9:125-36 (1987).

Others have recognized this stability problem associated with such UV-A absorbers, and have attempted to find means of stabilizing such compounds. See, e.g., U.S. Patent 5,783,173 (using alkylbenzoates), 5,993,789 (using diester and/or polyesters of naphthalene dicarboxylic acids), U.S. Patent No. 5,346,691, PCT Application No. WO98/00099, and European Patent No.

- 2 -

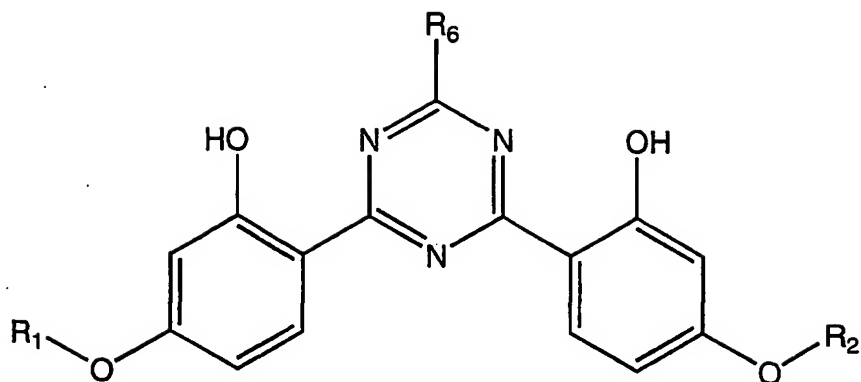
845,260 (using trianilino triazine derivatives with or without derivatives of diphenylcyanoacrylic acid), and U.S. Patent Nos. 5,576,354 and 6,033,649 (using α -cyano- β,β -diphenyl-acrylate stabilizer), and European Patent
5 Nos. 514,491, 685,222, and 685,225 (using octocrylene, homomenthyl salicylate, octyl salicylate, and 4-methyl benzylidene camphor to stabilize avobenzene).

The present invention relates to the discovery that certain triazine derivatives surprisingly stabilized
10 dibenzoylmethane derivative UV-A absorbers, even in the presence of octyl methoxycinnamate, a commonly used UV-B absorber known to increase photo-instability of such UV-A absorbers.

15 **SUMMARY OF THE INVENTION**

In one aspect, the invention features a composition comprising: (a) one or more dibenzoylmethane derivative UV-A absorbing agent(s) and (b) one or more triazine derivative(s). What is meant by a triazine derivative is
20 a compound comprising one or more triazine group(s) and capable of absorbing radiation in the UV-A range (e.g., from about 290 to about 320 nm). In one embodiment, the triazine derivative is of formula (I)

- 3 -

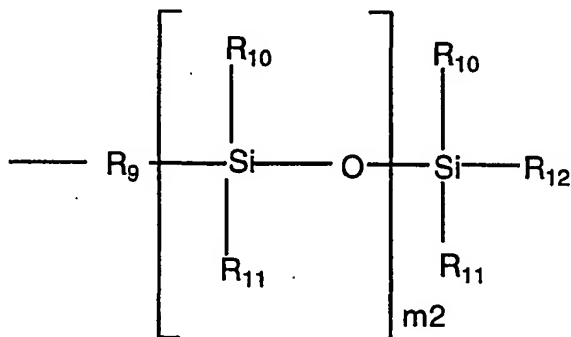


(I)

wherein,

5 R_1 and R_2 , independently, are C_3 - C_{18} alkyl, C_2 - C_{18} alkenyl, a radical of the formula $-CH_2-CH(OH)-CH_2-O-R_8$, or a radical of the formula (II)

(II)

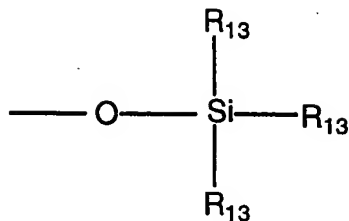


10 R_9 is a direct bond, C_1 - C_4 alkenyl, or a radical of the formula $-C_{m1}H_{2m1}-$ or $-C_{m1}H_{2m1}-O-$;

15 R_{10} , R_{11} , and R_{12} , independently, are C_1 - C_{18} alkyl, C_1 - C_{18} alkoxy, or a radical of the formula (III)

- 4 -

(III)



R_{13} is C_1 - C_5 alkyl;

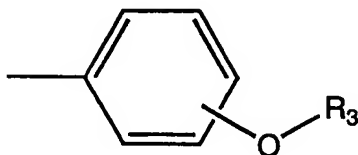
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m_1 is 1 to 4;

m_2 is 0 to 5;

R_6 is a radical of the formula (IV)

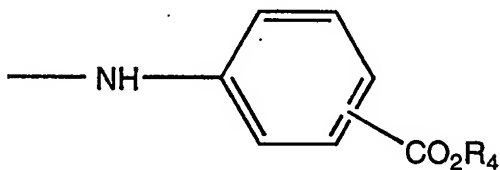
(IV)



10

or of the formula (V)

(V)

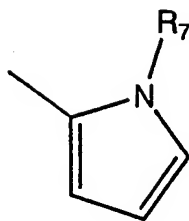


15

or of the formula (VI)

(VI)

- 5 -



R₃ is hydrogen, C₁-C₁₀ alkyl, or a radical of the formula $-(\text{CH}_2\text{CHR}_5-\text{O})_{m4}-\text{R}_4-\text{CH}_2$ or $-\text{CH}(\text{OH})-\text{CH}_2-\text{O}-\text{R}_8$;

R₄ is hydrogen, a metal cation, C₁-C₅ alkyl, or a radical of the formula $-(\text{CH}_2)_{m3}-\text{O}-\text{R}_8$;

R₅ is hydrogen or methyl;

R₈ is hydrogen or C₁-C₈ alkyl;

R₇ is C₁-C₁₈ alkyl;

m₃ is 1 to 4; and

m₄ is 1 to 16.

Examples of compounds of formula (I), and the synthesis thereof, are described in U.S. Patent No. 5,955,060.

In one embodiment, the triazine derivative of formula (I) is 2,4-Bis{[4-(2-ethyl-hexyloxy)-2-hydroxy]-phenyl}-6-(4-methoxyphenyl)-(1,3,5)-triazine.

In one embodiment, the triazine derivative is present in an amount sufficient to photo-stabilize the dibenzoylmethane derivative. What is meant by photo-stabilize is that the triazine derivative is present in an amount to reduce or eliminate the loss of UV-A absorbency of the composition containing the dibenzoylmethane derivative following exposure to UV radiation. In one embodiment, the triazine derivative is present in an amount sufficient to reduce the loss of

- 6 -

UV-A absorbency of the composition by about fifty percent following exposure to 33 J/cm² of full spectrum UV radiation). In one embodiment, the dibenzoylmethane derivative UV-A absorbing agent is present in an amount
5 from about 0.1% to about 20%, by weight, of the composition (e.g., about 1% to about 10%, by weight, of the composition) and the triazine derivative is present in an amount from about 0.1% to about 20%, by weight, of said composition (e.g., about 1% to about 10%, by
10 weight, of the composition).

The present invention also features a method of stabilizing a dibenzoylmethane derivative UV-A absorbing agent in a composition comprising adding to said composition an effective amount of a triazine
15 derivative. The present invention also features a method of protecting skin and hair from UV radiation comprising administering the above compositions.

Other features and advantages of the present invention will be apparent from the detailed description
20 of the invention and from the claims.

DETAILED DESCRIPTION OF THE INVENTION

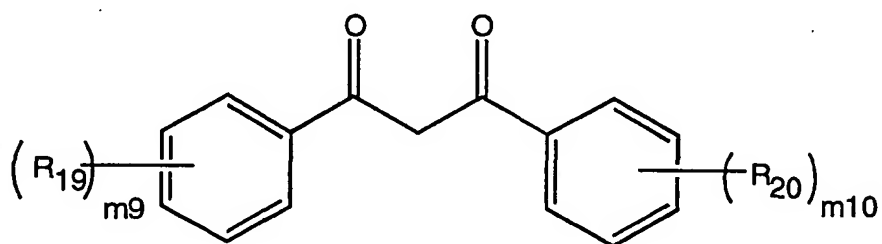
It is believed that one skilled in the art can, based upon the description herein, utilize the present
25 invention to its fullest extent. The following specific embodiments are to be construed as merely illustrative, and not limitative of the remainder of the disclosure in any way whatsoever.

- 7 -

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which the invention belongs. Also, all publications, patent applications, patents, and other references mentioned herein are incorporated by reference. As used herein, unless otherwise indicated, all alkyl, alkenyl, and alkoxy groups may be straight or branched chain groups.

The present invention relates to a method of stabilizing a dibenzoylmethane derivative UV-A absorbing agent. What is meant by a dibenzoylmethane UV-A absorbing agent is a compound comprising a dibenzoylmethane group and capable of absorbing radiation in the UV-A range (e.g., from about 320 to 400 nm). Examples of dibenzoylmethane derivative UV-A absorbing agent include those of the formula (VII):

(VII)



wherein R_{19} and R_{20} , independently, are $\text{C}_1\text{--C}_8$ alkyl or $\text{C}_1\text{--C}_8$ alkoxy, $m9$ is 0 to 3, and $m10$ is 1 to 3. Examples and the synthesis of such compositions are disclosed in U.S. Patent No. 4,489,057 and include, but are not limited

- 8 -

to, 4-(1,1-dimethylethyl)-4'-methoxydibenzoylmethane (avobenzene and sold as Parsol® 1789, Roche Vitamins and Fine Chemicals, Nutley, New Jersey, USA), 2-2-methyldibenzoylmethane, 4-methyl-dibenzoylmethane, 4-isopropyldibenzoylmethane, 4-tert-butyldibenzoylmethane, 4-tert-butyl-4'-methoxydibenzoylmethane, 2,4-dimethylbenzoylmethane, 2,5-dimethylbenzoylmethane, 4,4'-diisopropylbenzoylmethane, 2-methyl-5-isopropyl-4'-methoxydibenzoylmethane, 2-methyl-5-tert-butyl-4'-methoxydibenzoylmethane, 2,4-dimethyl-4'-methoxydibenzoylmethane, and 2,6-dimethyl-4-tert-butyl-4'-methoxydibenzoylmethane. In one embodiment, the dibenzoylmethane derivative can range from about 0.1% to about 20%, by weight, of the total composition (e.g., from about 1% to about 10%, by weight).

In one embodiment, the composition further comprises one or more additional UV-A and/or UV-B absorbing/reflecting agent(s). Examples of such absorbing/reflecting agents include, but are not limited to: methoxycinnamate derivatives such as octyl methoxycinnamate and isoamyl methoxycinnamate; camphor derivatives such as 4-methyl benzylidene camphor, camphor benzalkonium methosulfate, and terephthalylidene dicamphor sulfonic acid; salicylate derivatives such as octyl salicylate, trolamine salicylate, and homosalate; sulfonic acid derivatives such as phenylbenzimidazole sulfonic acid; benzene derivatives such as dioxybenzone, sulisobenzene, and oxybenzone; benzoic acid derivatives

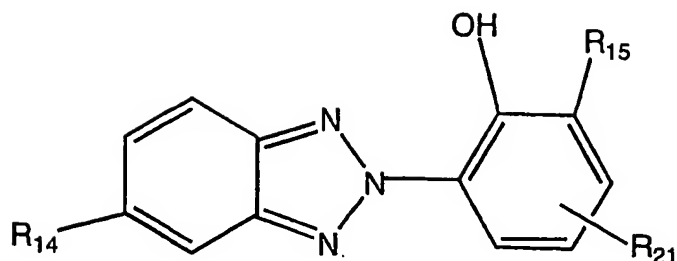
- 9 -

such as aminobenzoic acid and octyldimethyl para-amino benzoic acid; octocrylene; dioctyl butamido triazone, titanium dioxide; zinc oxide; iron oxides; octyl triazone; butyl methoxydibenzoyl methane; drometrizole trisiloxane; and menthyl anthranilate. Other UV absorbers/reflectors useful herein can be found in Sagarin, Cosmetics Science and Technology, Chapter VIII, pages 189 et seq. and the ICI Handbook page 1672. A list of such compounds is also disclosed in U.S. Patent Number 4,919,934. The individual UV absorbing/reflecting agent concentration can range from about 0.1% to about 30%, by weight, of the composition (e.g., from about 1% to about 20%, by weight). The total concentration of all such agents should be based on the desired sunscreen protection factor ("SPF") level (e.g., an SPF level of from about 10 to about 60).

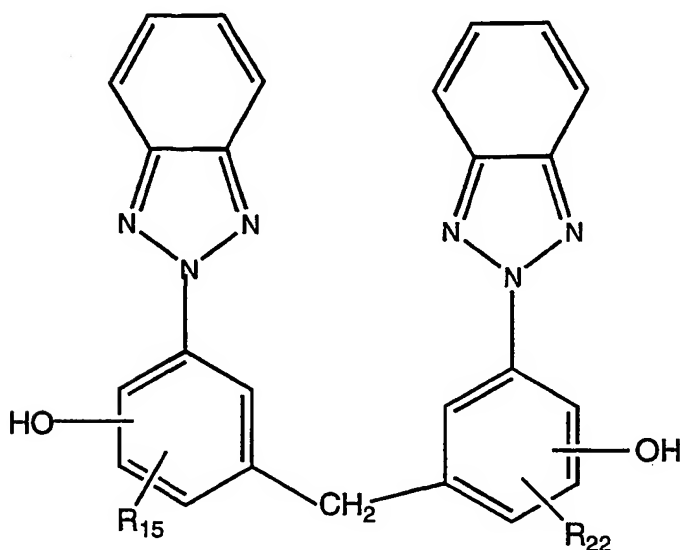
In one embodiment, the composition further comprises one or more triazole derivative(s). What is meant by a triazole derivative is a compound comprising one or more triazole groups. Examples of triazoles are compounds of the formulae (VIII) or (IX):

(VIII)

- 10 -



(IX)



5

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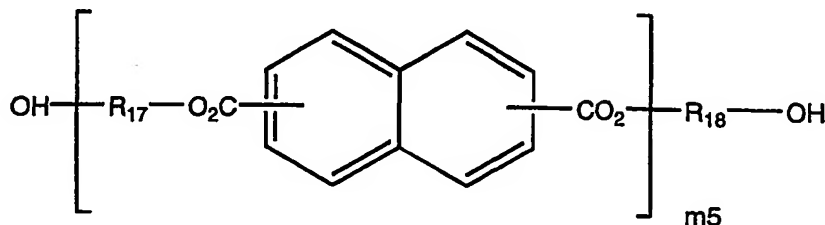
wherein R_{14} is C_1 - C_{18} alkyl or hydrogen; R_{15} and R_{22} , independently, are C_1 - C_{18} alkyl optionally substituted with a phenyl group, and R_{21} is C_1 - C_8 alkyl. Compounds of Formulae (VIII) and (IX) are describe in U.S. Patent No. 5,869,030, and include, but not limited to, methylene bis-benzotriazolyl tetramethylbutylphenol (Tinosorb M®, Ciba Specialty Chemicals Corporation, Greensboro, North Carolina, USA). In one embodiment, the triazole derivative can range from about 0.1% to about 20%, by

- 11 -

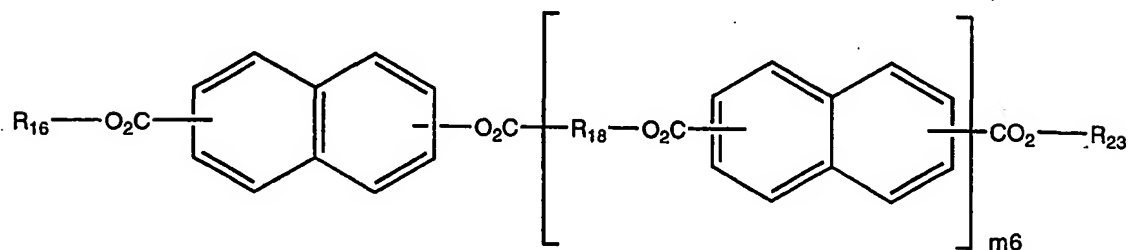
weight, of the total composition (e.g., from about 1% to about 10%, by weight).

In one embodiment, the composition further comprises a diester or polyester of a naphthalene dicarboxylic acid. Examples of diesters and polyesters of a naphthalene dicarboxylic acid are compounds of formulae (X) or (XI):

(X)



(XI)



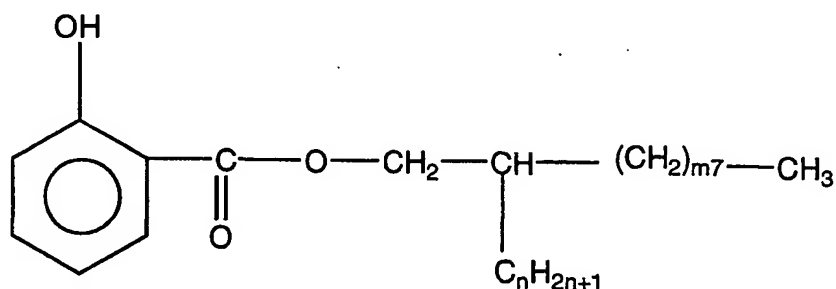
wherein R_{16} and R_{23} , independently, are selected from the group consisting of a C_1 - C_{22} alkyl, a diol having the structure $\text{HO}-\text{R}_{18}-\text{OH}$, and a polyglycol having the structure $\text{HO}-\text{R}_{17}-(-\text{O}-\text{R}_{18}-)_{m5}-\text{OH}$; R_{17} and R_{18} , independently, are C_1 - C_6 alkenyl; and $m5$ and $m6$, independently, are each in the range of 1 to about 100. Examples, including the synthesis, of such diesters or polyesters of naphthalene dicarboxylic acid are described in U.S. Patent No.

- 12 -

5,993,789, and include, but not limited to, diethylhexyl naphthalate (HallBrite® TQ, C.P. Hall Company, Bedford Park, Illinois, USA). See Bonda, et al., Allured's Cosmetic & Toiletries Magazine, 115(6):37-45 (2000) disclosing the uses of such compounds in sunscreen compositions. In one embodiment, the diester or polyester of a naphthalene dicarboxylic acid can range from about 0.1% to about 30%, by weight, of the total composition (e.g., from about 1% to about 10%, by weight).

In one embodiment, the composition further comprises an alkyl benzoate derivative. Examples of alkyl benzoate derivatives are compounds of the formulae (XII) or (XIII):

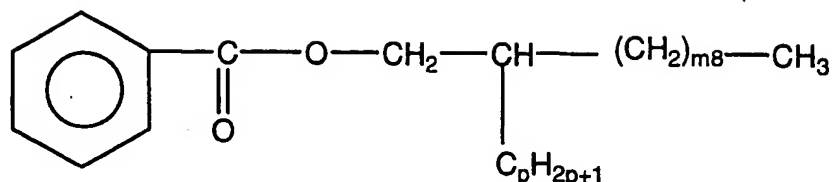
(XII)



wherein m7 is 5, 7, or 9 and n is 4, 6, or 8;

(XIII)

- 13 -



wherein $m8$ is 5 or 7 and p is 4 or 6.

5 The compounds of formulae (XII) and (XIII) may be formed by typical esterification and transesterification reactions, e.g., as describe in U.S. Patent No. 5,783,173. Examples of such long branched chain alkyl benzoates are listed in U.S. Patent No. 5,783,173 and
10 include, but not limited to, butyloctyl salicylate (HallBrite® BHB, C.P. Hall Company, Bedford Park, Illinois, USA). In one embodiment, the alkyl benzoate derivative can range from about 0.1% to about 30%, by weight, of the total composition (e.g., from about 1% to
15 about 10%, by weight).

In one embodiment, the compositions of the present invention further comprise one or more other cosmetically active agent(s). What is meant by a "cosmetically active agent" is a compound that has a
20 cosmetic or therapeutic effect on the skin, e.g., agents to treat wrinkles, acne, or to lighten the skin. In one embodiment, the agent is selected from, but not limited to, the group consisting of: hydroxy acids; benzoyl peroxide; sulfur resorcinol; D-panthenol; hydroquinone;
25 anti-inflammatory agents; skin lightening agents; antimicrobial and antifungal agents such a miconazole,

- 14 -

ketoconazole, and elubial; vitamins such as ascorbic acid; tocopherols and tocotrienols such as tocopheryl acetate; retinoids such retinol, retinal, retinyl palmitate, retinyl acetate, and retinoic acid; hormones such as estrogens and dihydroxyandrostene dione; 2-dimethylaminoethanol; lipoic acid; amino acids such a proline and tyrosine; lactobionic acid; self-tanning agents such as dihydroxy acetone; dimethyl aminoethanol; acetyl-coenzyme A; niacin; riboflavin; thiamin; ribose; electron transporters such as NADH and FADH₂; botanical extracts such as ginkgo biloba, aloe vera, and soy; and derivatives thereof. The cosmetically active agent will typically be present in the composition of the invention in an amount of from about 0.001% to about 20% by weight of the composition, e.g., about 0.01% to about 10% such as about 0.1% to about 5% by weight of the composition.

Examples of hydroxy acids include, but are not limited, to (i) alpha-hydroxy acids such as glycolic acid, lactic acid, malic acid, citric acid, and tartaric acid, (ii) beta-hydroxy acids such as salicylic acid, and/or (iii) polyhydroxy acids. See, e.g., European Patent Application No. 273,202.

Examples of derivatives of ascorbic acid include, but are not limited to, ascorbyl palmitate, magnesium ascorbyl phosphate, sodium ascorbyl phosphate, zinc ascorbyl phosphate, ascorbyl glucoside, sodium ascorbate, and ascorbyl polypeptide. An example of a

- 15 -

derivative of hydroquinone includes, but is not limited to, arbutin.

The compositions of the present invention may also comprise one or more of the following: antioxidants (e.g., ascorbic acid, tocopherols, polyphenols, tocotrienols, BHA, and BHT), chelating agents (e.g., EDTA), and preservatives (e.g., parabens). Examples of suitable antioxidants, preservatives, and chelating agents are listed in pp. 1612-13, 1626, and 1654-55 of the ICI Handbook. In addition, the topical compositions useful herein can contain conventional cosmetic adjuvants, such as dyes, opacifiers (e.g., titanium dioxide), pigments, and fragrances.

The compositions of the present invention can be used by topically administering it to a mammal, e.g., by the direct laying on or spreading of the composition on the skin or hair of a human. The cosmetic compositions useful in the subject invention, thus, involve formulations suitable for topical application to mammalian skin or hair, the formulation comprising (i) dibenzoylmethane derivative(s), (ii) the triazine derivative(s), (iii) optionally, other compounds/agents such as the other UV-A or UV-B absorbers/reflectors listed herein, and (iv) a cosmetically-acceptable topical carrier. The term "cosmetically-acceptable topical carrier" refers to a carrier for topical use that is capable of having the dibenzoylmethane and triazine derivative(s) and any other agents dispersed or

- 16 -

dissolved therein, and possessing acceptable safety properties.

The topical compositions useful in the present invention may be used for a variety of cosmetic uses, including, but not limited to, protection the skin or hair from UV radiation. The compositions, thus, may be made into a wide variety of product types. These include, but are not limited to lotions, creams, gels, sticks, sprays, ointments, mousses, and cosmetics/make-up. These products may comprise several types of carrier systems including, but not limited to single phase solutions (e.g., oil based solutions), emulsions, and gels.

The compositions of the present invention may be prepared using methodology that is well known by an artisan of ordinary skill. The following is a description of the manufacturing of cosmetic compositions of the present invention. Other compositions of the invention can be prepared in an analogous manner by a person of ordinary skill in the art.

Example 1: TESTING OF FORMULATIONS CONTAINING
DIBENZOYLMETHANE AND TRIAZINE DERIVATIVES

The sunscreen containing composition base of Table I was used in the following experiments to test the photostability of the formulations containing a dibenzoylmethane derivative UV-A absorber.

- 17 -

Table I

INGREDIENT	% (W/W)
WATER	q.s. 100
ACRYLATES C10-30 ALKYL ACRYLATE COPOLYMER	0.2
TRIETHANOLAMINE	0.65
DISODIUM EDTA	0.1
HOMOSALATE	12
OCTYL METHOXYCINNAMATE	7.5
OCTYL SALICYLATE	5
AVOBENZONE	3
CETYL PHOSPHATE	0.5
SORBITAN ISOSTEARATE	1.5
CETYL ALCOHOL	1.5
STEARIC ACID	1.5
ISOSTEARIC ACID	1.5
PRESERVATIVE MIXTURE	1.5

5 The acrylates C10-30 alkyl acrylate copolymer was
first dispersed in the water in a first container and
then neutralized with triethanolamine. The dispersion
was then heated to 80-85°C during which time the
disodium EDTA was added. The homosalate, octyl
methoxycinnamate, octyl salicylate, and avobenzone were
10 added to and mixed in a second container, and slowly
heated. Once the solution was clear, the remaining
ingredients were added to and mixed with the clear
solution. The preservative mixture was obtained from
Collaborative Group (East Setauket, New York, USA) under
15 the trade name Germazide® MPV. Once both phases reached
85°C, the ingredients in the second container were added
to the first container and mixed for ten minutes. The

- 18 -

resulting emulsion was then cooled to 45°C, and mixed in a homomixer for one minute.

To this formulation base, the following additional ingredients, in the amounts indicated in Table II, were added initially to the second container: 2,4-Bis{[4-(2-ethyl-hexyloxy)-2-hydroxy]-phenyl}-6-(4-methoxyphenyl)-(1,3,5)-triazine ("TS") (Tinosorb S®, Ciba Specialty Chemicals Corporation); diethylhexyl naphthalate ("TQ") (HallBrite TQ®, C.P. Hall Co.); and/or butyloctyl salicylate ("BHB") (HallBrite BHB®, C.P. Hall Co.):

Table II

FORMULATION NO.	ADDED INGREDIENT(S) (%W/W)
1	NONE
2	BHB (10%)
3	TQ (10%)
4	BHB(5%) + TQ (5%)
5	TS (2%)
6	TS (3%)
7	TS (2%) + TQ (10%)
8	TS (2%) + BHB(10%)
9	TS (2%) + TQ (5%) + BHB (5%)
10	TS (1.5%)
11	TS (1%)
12	TS (0.5%)
13	TS (0.25%)

These thirteen formulations were tested in the following in vitro photostability assay in which thin films of the formulations were applied to a substrate and measured for reduction in UV absorption properties following subjection to solar simulated UV radiation. First, the

- 19 -

solar simulator (Solar Light Solar Simulator Model 600S, Philadelphia, Pennsylvania, USA) was warmed up for 20 minutes prior to measurement of fluence rate. The baseline transmission of the Vitro Skin™ samples (IMS, Milford, Connecticut) were measured without application of the formulation (n=5 per sample). The formulations were then applied to the Vitro Skin™ samples at an application density of 2 mg/cm² and spread uniformly over the surface of the sample. The samples were then allowed to dry for 20 minutes before measurement of UV-A absorbance using calibrated Labsphere™ UV-1000S UV transmission analyzer (Labsphere, North Sutton, New Hampshire, USA). The fluence rate of the solar simulator was measured for the full UV spectrum in terms of W/cm². The samples were then exposed to 0, 20, and 50 J/cm² of full spectrum radiation from the solar simulator, and then the absorbance of the samples were re-measured. The percent UV-A protection lost following the various amount of radiation exposure are indicated in Table III.

Table III

FORMULATION NO.	0 J/CM ²	20 J/CM ²	50 J/CM ²
1	0%	23%	55%
2	0	26	57
3	0	22	44
4	0	19	41

- 20 -

5	0	13	23
6	0	2	16
7	0	8	16
8	0	5	14
9	0	10	21
10	0	8	14
11	0	13	31
12	0	14	27
13	0	17	27

As indicated in Table III, the UV-A protection afforded by the dibenzoylmethane derivative UV-A absorber avobenzene in Formulation No. 1 substantially degraded 23% and 55% as a result of poor photostability following exposure to, respectively, 20 Joules and 50 Joules of radiation. As seen in Formulation Nos. 2, 3, and 4, BHB and TQ, alone or in combination, were also ineffective in stabilizing avobenzene, resulting degradation of UV-A protection of between 19%- 26% and 41%-57% following exposure to, respectively, 20 Joules and 50 Joules of radiation. TS, however, was found to surprisingly enhance the photostability of avobenzene. Formulation No. 5, containing 2% of TS, only degraded 13% and a 23% following exposure to, respectively, 20 Joules and 50 Joules of radiation. Formulation No. 6, containing 3% of TS, even more surprising, only degraded 2% and a 16% following exposure to, respectively, 20 Joules and 50 Joules of radiation. As seen in Formulation Nos. 6, 7,

- 21 -

8, and 9, BHB and TQ, alone or in combination, further enhanced the stability of the dibenzoylmethane derivative UV-A absorber containing composition. Formulation Nos. 10-13, containing only between 1.5% and 0.25% TS also showed reduced degradation of UV-A absorbency as compared to Formulation No. 1.

Example 2: TESTING OF FORMULATIONS CONTAINING
DIBENZOYLMETHANE AND TRIAZINE DERIVATIVES

Similar studies were run using different oil-in-water emulsions of Table IV containing the dibenzoylmethane derivative UV-A absorbing agent at either 2 or 2.5% (W/W), octyl methoxycinnamate at either 4% or 6% (W/W), and TS at either 1%, 2%, and 4% (W/W).

Table IV

INGREDIENT	% (W/W)
GLYCERYL STEARATE/PEG100 STEARATE 50/50	0.7
CYCLOMETHICONE	3
C12-15 ALKYL BENZOATE	4
BUTYROSPERMUM PARKII	0.5
OCTYL METHOXYCINNAMATE	SEE ABOVE
4-METHYL BENZYLIDENE CAMPHOR	2
BUTYLMETHOXY DIBENZOYLMETHANE	SEE ABOVE
TS	SEE ABOVE
PROPYL PARABEN	0.07
PVP/HEXADECENE COPOLYMER	0.15
WATER	Q.S. 100
CARBOMER	0.2
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	0.4
TROMETHAMINE	0.456
DISODIUM EDTA	0.1

- 22 -

METHYL PARABEN	0.2
PHENOXYETHANOL	0.73
BUTYLENE GLYCOL	3
GLYCERIN	2
DIMETHICONE COPOLYOL POLYACRYLATE	0.5
ACRYLATE COPOLYMER	2
ALCOHOL (96°)	2.5
TOCOPHERYL ACETATE	0.5
NYLON-12	1
COLORANTS	0.0022

The Glyceryl Stearate/PEG100 Stearate 50/50
(Simulsol 165V, Seppic, Paris, France) Cyclomethicone,
C12-15 alkyl benzoate, Butyrospermum Parkii (Cetiol
5 SB45, Cognis, Dusseldorf, Germany), Octyl
Methoxycinnamate, 4-Methylbenzylidene camphor,
Butylmethoxy dibenzoylmethane, TS, Propyl paraben, and
PVP hexadecene copolymer were mixed together in a first
beaker and heated to 85°C. The carbomer and the
10 acrylate C10-30 alkyl acrylate crosspolymer (Pemulen TR-
1, BF Goodrich, Brecksville, Ohio, USA) were then
dispersed in the water in a second beaker and stirred
vigorously. The mixture was then heated to 40°C and
then neutralized with the tromethamine. Next, the
15 disodium EDTA, methyl paraben, phenoxyethanol, butylene
glycol, glycerin, and dimethicone copolyol polyacrylate,
and acrylate copolymer was added to the second beaker.
The second beaker was then heated to 75°C. The mixture
in the first beaker was then added to the second beaker
20 and stirred. The resulting emulsion was then allowed to

- 23 -

cool to 35°C after which time the remaining ingredients were added.

Six formulations, described below, were then tested for their percent UV-A protection lost ("% Loss") following exposure to 33 J/cm² of UV radiation.

Table V

FORM. NO.	AVOBENZONE (W/W)	TS (W/W)	OMC (W/W)	% LOSS
1	2%	0%	4%	27.3%
2	2	1	4	8.5
3	2	2	4	0
4	2	4	4	0
5	2.5	0	6	51
6	2.5	1	6	7.7

The following method was used to determine % UV-A protection loss from the above six formulations:

In vitro photostability assays were performed using a protocol similar to the one previously described in Example 1 except that that thin film of the above formulations were applied to quartz plate, the solar simulator used was a 150W Xenon Lamp Model 66011 (Oriel Instruments, Stratford, Connecticut, USA), providing 33J/cm² full spectrum radiation, and the absorbance was measured by a Spectroradiometer Model 752 (Optronic Laboratories, Orlando, Florida, USA). The percent UV-A protection lost following full spectrum UV exposure are indicated Table V.

- 24 -

As in Example 1, this Example 2 also found, as indicated in Table V, that the triazine derivative TS surprisingly was able to photostabilize the dibenzoylmethane derivative avobenzone. For example, adding 1%, by weight, of TS reduced the loss of UV-A protection afforded by the composition from 27.3% to only 8.5% (comparing Formulation Nos. 1 and 2). The further addition to either 2% or 4%, by weight, eliminated any loss of UV-A protection (comparing Formulation No. 1 to Formulation Nos. 3 or 4). Similarly, the addition of 1%, by weight, of TS reduced the loss of UV-A protection from a composition containing 2.5% avobenzone from 51% to only 7.7% (comparing Formulation No. 5 and 6).

Example 3: FORMULATION CONTAINING DIBENZOYLMETHANE AND TRIAZINE DERIVATIVES

The following cosmetic composition containing the ingredients listed below in Table VI was made in a manner as set forth in Example 2:

Table VI

INGREDIENT	% (W/W)
PEG-100 STEARATE/GLYCERYL STEARATE	0.7
TOCOPHERYL ACETATE	0.5
PROPYL PARABEN	0.07
PVP/HEXADECENE COPOLYMER	0.15
DISODIUM EDTA	0.1
BUTYROSPERMUM PARKII	0.5

- 25 -

C12-15 ALKYL BENZOATE	4
OCTYL METHOXYCINNAMATE	2
4-METHYL BENZYLIDENE CAMPHOR	4
TS	1
BUTYLMETHOXY DIBENZOYLMETHANE	2
WATER	Q.S. 100
CARBOMER	0.2
ACRYLATES/C10-30 ALKYL ACRYLATE CROSSPOLYMER	0.4
BUTYLENE GLYCOL	3
TROMETHAMINE	0.456
METHYL PARABEN	0.2
PHENOXYETHANOL	0.73
GLYCERIN	2
CYCLOMETHICONE	3
DIMETHICONE COPOLYOL POLYACRYLATE	0.5
ACRYLATES COPOLYMER	2
ALCOHOL	2.5
NYLON-12	1
COLORANT	0.0022

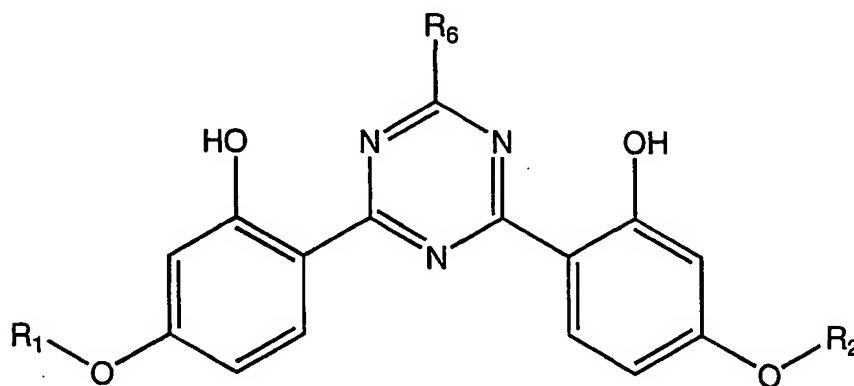
5 It is understood that while the invention has been described in conjunction with the detailed description thereof, that the foregoing description is intended to illustrate and not limit the scope of the invention, which is defined by the scope of the appended claims. Other aspects, advantages, and modifications are within the claims.

- 26 -

What is claimed is:

1. A composition comprising:

- 5 (a) a dibenzoylmethane derivative UV-A absorbing agent; and
(b) a triazine derivative of formula (I)



(I)

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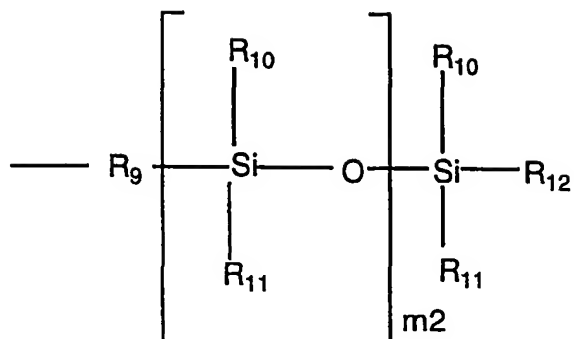
wherein,

R₁ and R₂, independently, are C₃-C₁₈ alkyl, C₂-C₁₈ alkenyl, a radical of the formula -CH₂-CH(OH)-CH₂-O-R₈, or a radical of the formula (II)

15

(II)

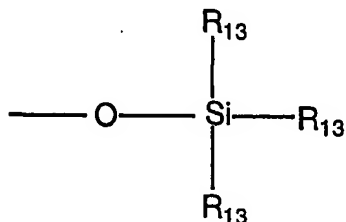
- 27 -



R₉ is a direct bond, C₁-C₄ alkenyl, or a radical of the formula -C_{m1}H_{2m1}- or -C_{m1}H_{2m1}-O-;

5 R₁₀, R₁₁, and R₁₂, independently, are C₁-C₁₈ alkyl, C₁-C₁₈ alkoxy, or a radical of the formula (III)

(III)



10

R₁₃ is C₁ -C₅ alkyl;

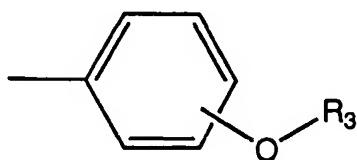
m₁ is 1 to 4;

m₂ is 0 to 5;

R₆ is a radical of the formula (IV)

15

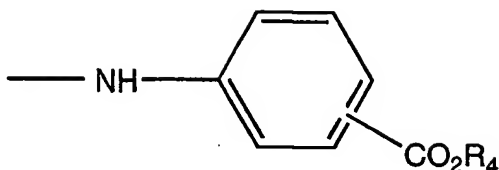
(IV)



- 28 -

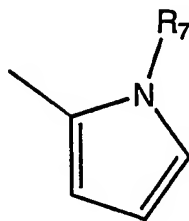
or of the formula (V)

(V)



5 or of the formula (VI)

(VI)



10 R_3 is hydrogen, C_1 - C_{10} alkyl, or a radical of the formula $-(CH_2CHR_5-O)_{m_4}-R_4-CH_2$ or $-CH(OH)-CH_2-O-R_8$;

R_4 is hydrogen, a metal cation, C_1 - C_5 alkyl, or a radical of the formula $-(CH_2)_{m_3}-O-R_8$;

R_5 is hydrogen or methyl;

15 R_8 is hydrogen or C_1 - C_8 alkyl;

R_7 is C_1 - C_{18} alkyl;

m_3 is 1 to 4; and

m_4 is 1 to 16.

20

2. The composition of claim 1 wherein said dibenzoylmethane derivative UV-A absorbing agent is

- 29 -

selected from the group consisting of: 2-methyldibenzoylmethane, 4-methyl-dibenzoylmethane, 4-isopropyldibenzoylmethane, 4-tert-butyldibenzoylmethane, 2,4-dimethylbenzoylmethane, 4-tert-butyl-4'-methoxy-dibenzoylmethane, 2,5-dimethylbenzoylmethane, 4,4'-diisopropylbenzoylmethane, 2-methyl-5-isopropyl-4'-methoxydibenzoylmethane, 2-methyl-5-tert-butyl-4'-methoxydibenzoylmethane, 2,4-dimethyl-4'-methoxydibenzoylmethane, and 2,6-dimethyl-4-tert-butyl-4'-methoxydibenzoylmethane.

3. The composition of claim 1 wherein said dibenzoylmethane derivative UV-A absorbing agent is 4-tert-butyl-4'-methoxydibenzoylmethane.

4. The composition of claim 1 wherein said triazine derivative of formula (I) is 2,4-Bis{[4-(2-ethyl-hexyloxy)-2-hydroxy]-phenyl}-6-(4-methoxyphenyl)-(1,3,5)-triazine.

5. The composition of claim 3 wherein said triazine derivative of formula (I) is 2,4-Bis{[4-(2-ethyl-hexyloxy)-2-hydroxy]-phenyl}-6-(4-methoxyphenyl)-(1,3,5)-triazine.

6. The composition of claim 1, wherein said dibenzoylmethane derivative UV-A absorbing agent is present in an amount from about 0.1% to about 20%, by

- 30 -

weight, of said composition and said triazine derivative is present in an amount from about 0.1% to about 20%, by weight, of said composition.

5 7. The composition of claim 5, wherein said 4-tert-butyl-4'-methoxydibenzoylmethane is present in an amount from about 0.1% to about 20%, by weight, of said composition and said 2,4-Bis{[4-(2-ethyl-hexyloxy)-2-hydroxy]-phenyl}-6-(4-methoxyphenyl)-(1,3,5)-triazine is
10 present in an amount from about 0.1% to about 20%, by weight, of said composition.

 8. The composition of claim 1 further comprising a UV-B absorbing agent.

15

 9. The composition of claim 8 wherein said UV-B absorbing agent is selected from the group consisting of methyl benzylidene camphor, octyl salicylate, phenylbenzimidazole sulfonic acid, homosalate, titanium
20 dioxide, zinc oxide, dioxybenzone, sulisobenzene, oxybenzone, and dioctyl butamido triazone.

 10. The composition of claim 8 wherein said composition comprises octyl methoxycinnamate.

25

 11. The composition of claim 8 wherein said UV-B absorbing agent is present in an amount from about 0.1%, to about 20%, by weight, of said composition.

- 31 -

12. The composition of claim 1, wherein said composition further comprises an alkyl benzoate derivative.

5

13. The composition of claim 12, wherein said alkyl benzoate derivative is butyloctyl salicylate.

10

14. The composition of claim 1, wherein said composition further comprises a diester or polyester derivative of a naphthalene dicarboxylic acid.

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15. The composition of claim 14, wherein said diester or polyester derivative of a naphthalene dicarboxylic acid is diethylhexyl naphthalate.

20

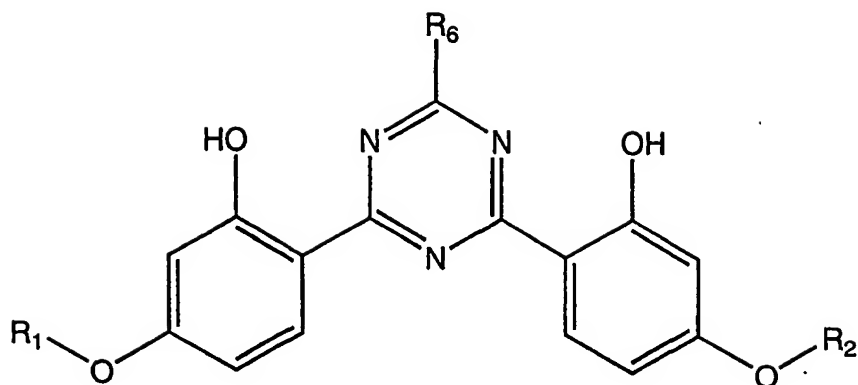
16. The composition of claim 12, wherein said composition further comprises a diester or polyester derivative of a naphthalene dicarboxylic acid.

17. The composition of claim 16, wherein said diester or polyester derivative of a naphthalene dicarboxylic acid is diethylhexyl naphthalate.

25

18. A method of stabilizing a dibenzoylmethane derivative UV-A absorbing agent in a composition, said method comprising adding to said composition an effective amount of a triazine derivative of formula (I)

- 32 -

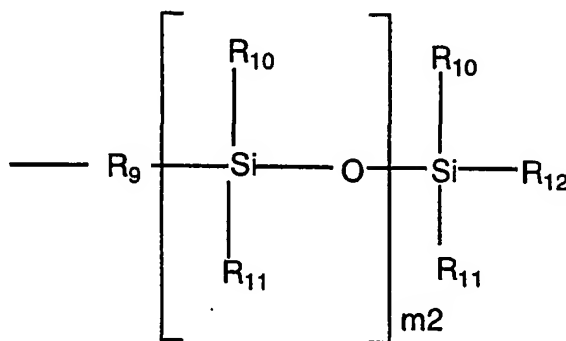


(I)

wherein,

- 5 R_1 and R_2 , independently, are C_3 - C_{18} alkyl, C_2 - C_{18} alkenyl, a radical of the formula $-\text{CH}_2-\text{CH}(\text{OH})-\text{CH}_2-\text{O}-R_8$, or a radical of the formula (II)

(II)



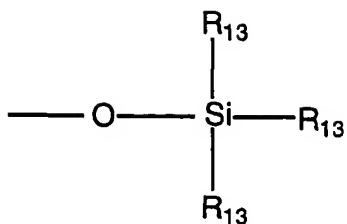
10

R_9 is a direct bond, C_1 - C_4 alkenyl, or a radical of the formula $-\text{C}_{m1}\text{H}_{2m1}-$ or $-\text{C}_{m1}\text{H}_{2m1}-\text{O}-$;

- 15 R_{10} , R_{11} , and R_{12} , independently, are C_1 - C_{18} alkyl, C_1 - C_{18} alkoxy, or a radical of the formula (III)

- 33 -

(III)



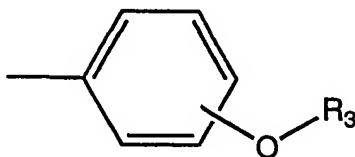
R_{13} is C_1 - C_5 alkyl;

m_1 is 1 to 4;

m_2 is 0 to 5;

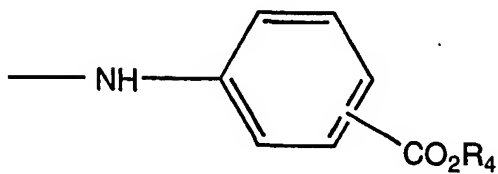
R_6 is a radical of the formula (IV)

(IV)



or of the formula (V)

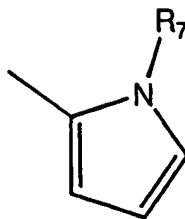
(V)



or of the formula (VI)

(VI)

- 34 -



R₃ is hydrogen, C₁-C₁₀ alkyl, or a radical of the formula $-(\text{CH}_2\text{CHR}_5-\text{O})_{m4}-\text{R}_4-\text{CH}_2$ or $-\text{CH}(\text{OH})-\text{CH}_2-\text{O}-\text{R}_8$;

R₄ is hydrogen, a metal cation, C₁-C₅ alkyl, or a radical of the formula $-(\text{CH}_2)_{m3}-\text{O}-\text{R}_8$;

R₅ is hydrogen or methyl;

R₈ is hydrogen or C₁-C₈ alkyl;

R₇ is C₁-C₁₈ alkyl;

m₃ is 1 to 4; and

m₄ is 1 to 16.

19. The method of claim 18, wherein said dibenzoylmethane derivative UV-A absorbing agent is 4-tert-butyl-4'-methoxydibenzoylmethane.

20. The method of claim 19, wherein said triazine derivative of formula (I) is 2,4-Bis{[4-(2-ethylhexyloxy)-2-hydroxy]-phenyl}-6-(4-methoxyphenyl)-(1,3,5)-triazine.

21. A method of protecting mammalian skin or hair from UV radiation comprising topically applying to the skin or hair a composition of claim 1.

INTERNATIONAL SEARCH REPORT

 Int: Application No
 PCT/EP 01/09932

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K7/42

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 897 715 A (BEIERSDORF AG) 24 February 1999 (1999-02-24) claims 1-5; example 4 ----	1-17,21
X	DE 197 26 121 A (BEIERSDORF AG) 24 December 1998 (1998-12-24) claims 1-9; examples 2,8,9 ----	1-17,21
X	EP 0 922 447 A (BEIERSDORF AG) 16 June 1999 (1999-06-16) claims 1-10; examples 7-9 ----	1-17,21
X	DE 197 56 376 A (BEIERSDORF AG) 24 June 1999 (1999-06-24) claims 1-6; example 9 ----- -/--	1-17,21

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

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INTERNATIONAL SEARCH REPORT

Inté Application No
PCT/EP 01/09932

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 970 688 A (BEIERSDORF AG) 12 January 2000 (2000-01-12) claims 1-8; example 8 ---	1-17,21
X	DE 198 33 634 A (BEIERSDORF AG) 3 February 2000 (2000-02-03) claims 1-8; example 2 ---	1-17,21
P,X	EP 1 034 778 A (BEIERSDORF AG) 13 September 2000 (2000-09-13) claims 1-5; example 3 -----	1-17,21

INTERNATIONAL SEARCH REPORT

Intel Application No
PCT/EP 01/09932

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
EP 897715	A	24-02-1999	DE	19735901 A1	25-02-1999
			EP	0897715 A2	24-02-1999
DE 19726121	A	24-12-1998	DE	19726121 A1	24-12-1998
EP 922447	A	16-06-1999	DE	19751221 A1	20-05-1999
			DE	19756377 A1	24-06-1999
			EP	0922447 A2	16-06-1999
DE 19756376	A	24-06-1999	DE	19756376 A1	24-06-1999
			EP	0935959 A2	18-08-1999
EP 970688	A	12-01-2000	DE	19830461 A1	13-01-2000
			EP	0970688 A2	12-01-2000
DE 19833634	A	03-02-2000	DE	19833634 A1	03-02-2000
			WO	0006113 A1	10-02-2000
			EP	1100452 A1	23-05-2001
EP 1034778	A	13-09-2000	DE	19910477 A1	14-09-2000
			EP	1034778 A2	13-09-2000
			JP	2000309520 A	07-11-2000